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☐ 1. Document ID: US 6147106 A

L2: Entry 1 of 14 File: USPT Nov 14, 2000

US-PAT-NO: 6147106
DOCUMENT-IDENTIFIER: US 6147106 A
TITLE: Indolinone combinatorial libraries and related products and methods for the treatment of disease

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 2. Document ID: US 6025157 A

L2: Entry 2 of 14 File: USPT Feb 15, 2000

US-PAT-NO: 6025157
DOCUMENT-IDENTIFIER: US 6025157 A
TITLE: Neurturin receptor

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 3. Document ID: US 6025192 A

L2: Entry 3 of 14 File: USPT Feb 15, 2000

US-PAT-NO: 6025192
DOCUMENT-IDENTIFIER: US 6025192 A
TITLE: Modified retroviral vectors

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 4. Document ID: US 5998187 A

L2: Entry 4 of 14 File: USPT Dec 7, 1999

US-PAT-NO: 5998187
DOCUMENT-IDENTIFIER: US 5998187 A
TITLE: Receptor tyrosine kinase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 5. Document ID: US 5910426 A

L2: Entry 5 of 14 File: USPT Jun 8, 1999

US-PAT-NO: 5910426
DOCUMENT-IDENTIFIER: US 5910426 A
TITLE: Protein tyrosine kinase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 6. Document ID: US 5882923 A

L2: Entry 6 of 14 File: USPT Mar 16, 1999

US-PAT-NO: 5882923
DOCUMENT-IDENTIFIER: US 5882923 A
TITLE: Glial cell line-derived neurotrophic factor regulation of ureteric budding and growth

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 7. Document ID: US 5852184 A

L2: Entry 7 of 14 File: USPT Dec 22, 1998

US-PAT-NO: 5852184
DOCUMENT-IDENTIFIER: US 5852184 A
TITLE: Protein tyrosine kinase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 8. Document ID: US 5821069 A

L2: Entry 8 of 14 File: USPT Oct 13, 1998

US-PAT-NO: 5821069
DOCUMENT-IDENTIFIER: US 5821069 A
TITLE: Method for determining tyrosine kinase in a sample

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw. Desc | Image

☐ 9. Document ID: US 5808036 A

L2: Entry 9 of 14 File: USPT Sep 15, 1998

US-PAT-NO: 5808036
DOCUMENT-IDENTIFIER: US 5808036 A
TITLE: Stem-loop oligonucleotides containing parallel and antiparallel binding domains

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 10. Document ID: US 5716818 A

L2: Entry 10 of 14 File: USPT Feb 10, 1998

US-PAT-NO: 5716818
DOCUMENT-IDENTIFIER: US 5716818 A
TITLE: Protein tyrosine kinase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 11. Document ID: US 5681714 A

L2: Entry 11 of 14 File: USPT Oct 28, 1997

US-PAT-NO: 5681714
DOCUMENT-IDENTIFIER: US 5681714 A
TITLE: Nucleic acid encoding tek receptor tyrosine kinase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 12. Document ID: US 5658791 A

L2: Entry 12 of 14 File: USPT Aug 19, 1997

US-PAT-NO: 5658791
DOCUMENT-IDENTIFIER: US 5658791 A
TITLE: Antibodies which specifically bind to proteins having tyrosine kinase activity, wherein said proteins have more than one tyrosine kinase domain, and no SH2 domains

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 13. Document ID: US 5514546 A

L2: Entry 13 of 14 File: USPT May 7, 1996

US-PAT-NO: 5514546
DOCUMENT-IDENTIFIER: US 5514546 A
TITLE: Stem-loop oligonucleotides containing parallel and antiparallel binding domains

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 14. Document ID: US 5466596 A

L2: Entry 14 of 14 File: USPT Nov 14, 1995

US-PAT-NO: 5466596
DOCUMENT-IDENTIFIER: US 5466596 A
TITLE: Tissue specific transcriptional regulatory element

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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ANTIBODYS.USPT.	13
ANTIBODIES.USPT.	36506
ANTIBODY.USPT.	37670
ANTIBODYS.USPT.	13
(1 AND (ANTIBODY OR ANTIBODIES)).USPT.	14

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L3: Entry 1 of 1 File: USPT Feb 15, 2000

DOCUMENT-IDENTIFIER: US 6025157 A
TITLE: Neurturin receptor

BSPR:
Aberrant expression of receptor tyrosine kinases ("RTK") correlates with transforming ability. For example, carcinomas of the liver, lung, breast and colon show elevated expression of Eph RTK. Unlike many other tyrosine kinases, this elevated expression can occur in the absence of gene amplification or rearrangement. Moreover, Hek, a human RTK, has been identified as a leukemia-specific marker present on the surface of a pre-B cell leukemia cell line. As with Eph, Hek also was overexpressed in the absence of gene amplification or rearrangements in, for example, hemopoietic tumors and lymphoid tumor cell lines. Over-expression of Myk-1 (a murine homolog of human Htk (Bennett et al., J Biol. Chem., 269(19):14211-8 (1994)) was found in the undifferentiated and invasive mammary tumors of transgenic mice expressing the Ha-ras oncogene. (Andres et al., Oncogene, 9(5): 1461-7 (1994) and Andres et al, Oncogene, 9(8):2431 (1994)). Ret, the product of the c-ret proto-oncogene, is a member of the receptor tyrosine kinase superfamily.

DEPR:
The present invention also provides for assay systems for detecting NTN activity, comprising cells which express high levels of NTNR.alpha., and which are, therefore, extremely sensitive to even very low concentrations of NTN or NTN-like molecules. The present invention provides for assay systems in which NTN activity or activities similar to NTN activity resulting from exposure to a peptide or non-peptide compound may be detected by measuring a physiological response to NTN in a cell or cell line responsive to NTN which expresses the NTNR.alpha. molecules of the invention. A physiological response may comprise any of the biological effects of NTN, including but not limited to, those described herein, as well as the transcriptional activation of certain nucleic acid sequences (e.g. promoter/enhancer elements as well as structural genes), NTN-related processing, translation, or phosphorylation, the induction of secondary processes in response to processes directly or indirectly induced by NTN, including Ret-mediated effects, and morphological changes, such as neurite sprouting, or the ability to support the survival of cells, for example, nodose or dorsal root ganglion cells, motoneurons, dopaminergic neurons, sensory neurons, Purkinje

cells, or hippocampal neurons.

DEPR:
Since NTNR.alpha., like GDNFR.alpha., lacks a cytoplasmic domain and appears to be anchored to the outer surface of the cell via GPI, transmission of the NTN signals to the cell interior must involve additional proteins. As the tyrosine kinase receptor Ret, which by itself does not bind GDNF or NTN with a high affinity (Jing et al. Cell 85:1113-1124 (1996)); Treanor et al. Nature 382:80-83 (1996); data not shown), appears to be a signaling component of the GDNF receptor, Ret transduction of the NTN response following binding of NTN to NTNR.alpha. was determined. To assay for tyrosine phosphorylation, cells were incubated for 1 h at 37.degree. C. with or without PIPLC, and then exposed to various concentrations of NTN. Cells were then removed from the plates with 2 mM EDTA in PBS and lysed with ice-cold buffer (10 mM sodium phosphate (pH 7.0), 100 mM NaCl, 1% NP40, 5 mM EDTA, 100 mM sodium vanadate, 2 mM PMSF, and 0.2 units of aprotinin), and used for immunoprecipitation with antisera raised against the 19 amino acid carboxyl terminus of Ret, followed by binding to protein A sepharose. The immunoprecipitated proteins were released by boiling in SDS sample buffer, separated on an 8% SDS-polyacrylamide gel, transferred to a nitrocellulose membrane, and reacted with anti-phosphotyrosine antibody (Upstate Biotechnology, Inc.); detection was with an ECL Western blotting detection system (Amersham Life Science). The human neuroblastoma cell line, TGW-1, which expresses endogenous c-ret (Ikeda et al. Oncogene 5:1291 (1990); Takahashi et al. Oncogene 6:297 (1991)), was exposed to NTN for 5 minutes, and the level of Ret tyrosine phosphorylation was determined. NTN clearly induced phosphorylation of Ret (FIG. 7D), as well as of the receptor tyrosine kinase responsive, cytoplasmic kinase ERK (i.e., MAPK) in this cell line (FIG. 7E), but not in 4 other neuroblastoma lines that were examined (data not shown). Furthermore, consistent with the hypothesis that NTNR.alpha. is an essential mediator between NTN and Ret, NTN failed to induce significant tyrosine phosphorylation on Ret in cells that were treated with PIPLC (FIG. 7F). A similar result was obtained with GDNF. Tyrosine-phosphorylated RET protein was readily detected in PIPLC-treated TGW-1 cell when NTN was added together with a soluble NTNR.alpha..

DEPR:
Since these findings herein suggested that Ret participates in the transmission of the NTN signal, it was determined whether Ret is part of a putative NTN receptor complex. To examine the formation of protein complexes upon exposure to NTN, co-immunoprecipitation experiments were done NTNR.alpha.-expressing TGW-1 cells exposed to 500 ng/ml of NTN. After exposure, cells were lysed a mild detergent brij 96 (Sigma) (Davis et al. 1993). For mammalian protein expression the complete open reading frame was amplified using PCR and cloned into a CMV based expression vector. For co-precipitation experiments, an epitope tag was inserted between the signal peptide and the mature coding sequence of NTNR.alpha.. When protein complexes were immunoprecipitated with a polyclonal

antibody to Ret and then analyzed on a western blot using a polyclonal antibody to NTN, NTN was readily co-immunoprecipitated by Ret antibodies, which is consistent with the notion that NTN and Ret physically interact on the cell surface. To confirm that NTNR.alpha. is part of the NTN/Ret protein complex, human embryonic kidney 293 cells were transiently transfected with expression vectors, Ret alone or with a combination of expression vectors for c-ret and an epitope tagged NTNR.alpha., exposed to NTN, and lysed with a mild detergent brij 96 (Sigma) (Davis et al. 1993). Putative immune complexes were immunoprecipitated with a polyclonal antibody against Ret, transferred onto a nitrocellulose filter, and analyzed with a polyclonal antibody against the epitope tagged NTNR.alpha.. In agreement with the idea that NTNR.alpha. and Ret can be found in a protein complex, NTNR.alpha., in the presence, but not in the absence of NTN was readily co-immunoprecipitated by Ret antibodies. These findings demonstrated that NTN, NTNR.alpha. and Ret can form a complex on the cell surface, that Ret and NTNR.alpha. are components of a functional NTN receptor, an that NTNR.alpha. is an intermediary in the interaction between NTN and Ret.

ORPL:
Trupp et al., "Functional receptor for GDNF encoded by the c-ret proto-oncogene" Nature381:785-789 (1996).

ORPL:
Trupp et al., "Functional receptor for GDNF encoded by the c-ret proto-oncogene" Nature 381:785-789 (1996).

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End of Result Set

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L4: Entry 6 of 6 File: USPT Nov 14, 1995

DOCUMENT-IDENTIFIER: US 5466596 A
TITLE: Tissue specific transcriptional regulatory element

BSPR:
In an embodiment of the invention, a method of determining the affect of a substance on cells of the endothelial lineage is provided comprising producing a transgenic non-human mammal characterized as having a plurality of cells containing a recombinant molecule comprising the transcriptional regulatory element of the invention operatively linked to a gene and a reporter gene encoding a phenotype which is not displayed by the mammal, or an ancestor of the mammal at an embryonic stage, comprising (a) introducing the recombinant molecule into a pronucleus of a mammalian zygote by microinjection, said zygote being capable of development into a mammal, thereby obtaining a genetically transformed zygote; (b) transplanting an embryo derived from the genetically transformed zygote into a pseudo-pregnant female capable of bearing the embryo to term and (c) isolating the embryo or allowing the embryo to develop to term, (d) assaying for the phenotype of the reporter gene in the embryo or transgenic non-human mammal to determine the pattern and extent of expression of the gene, and (e) determining the affect of the substance on cells of the endothelial lineage by

DEPR:
The reporter gene should be under the control of the transcriptional regulatory element and the pattern and extent of expression of the gene operatively linked to the transcriptional regulatory element may accordingly be determined in cells of the endothelial lineage. Preferably the reporter gene codes for a phenotype not displayed by the host cell and the phenotype may be assayed quantitatively. Examples of suitable reporter genes include lacZ (B-galactosidase), neo (neomycin phosphotransferase), cat (chloramphenicol acetyltransferase) dhfr (dihydrofolate reductase), aphIV (hygromycin phosphotransferase), lux (luciferase), uidA (B-glucuronidase). Preferably, the reporter gene is lacZ which codes for B-galactosidase. B-galactosidase may be assayed using the lactose analogue
X-gal(5-bromo-4-chloro3-indolyl-b-D-galactopyranoside) which is broken down by B-galactosidase to a product that is blue in color. (See for example Old R.W. & Primrose S.B., Principles of Gene Manipulation An Introduction to Genetic Engineering, 4th ed. Oxford University Press at pages 63-66 for a discussion of

procedures for screening for recombinants).

DEPR:
In an embodiment of the invention a method of determining the affect of a substance on cells of the endothelial lineage is provided comprising producing a transgenic non-human mammal characterized as having a plurality of cells containing a recombinant molecule comprising a transcriptional regulatory element of the invention linked to a gene encoding the substance, and a reporter gene encoding a phenotype which is not displayed by the mammal, or an ancestor of the mammal at an embryonic stage, comprising (a) introducing the recombinant molecule into a pronucleus of a mammalian zygote by microinjection, said zygote being capable of development into a mammal, thereby obtaining a genetically transformed zygote; (b) transplanting an embryo derived from the genetically transformed zygote into a pseudo-pregnant female capable of bearing the embryo to term and (c) if desired, allowing the embryo to develop to term, (d) assaying for the phenotype of the reporter gene in the embryo or transgenic mammal to determine the pattern and extent of expression of the gene, and (e) determining the affect of the substance on cells of the endothelial lineage by comparison to a standard.

DEPR:
As discussed above, the reporter gene should be under the control of the transcriptional regulatory element and accordingly the pattern and extent of expression of a gene operatively linked to the transcriptional regulatory element may be determined by assaying for the phenotype of the reporter gene. Preferably the reporter gene codes for a phenotype not displayed by the host cell and the phenotype may be assayed quantitatively. Examples of suitable reporter genes include lacZ (.beta.-galactosidase), neo (neomycin phophotransferase), cat (chloramphenicol acetyltransferase) dhfr (dihydrofolate reductase), aphIV (hygromycin phosphotransferase), lux (luciferase), uidA (.beta.-glucuronidase). Preferably, the reporter gene is lacZ which codes for .beta.-galactosidase. .beta.-galactosidase may be assayed using the lactose analogue X-gal(5-gromo-4-chloro-3-indolyl-.beta.-D-galactopyranoside) which is broken down by .beta.-galactosidase to a product that is blue in color. (See for example Old R. W. & Primrose S. B., Principles of Gene Manipulation An Introduction to Genetic Engineering, 4th ed. Oxford University Press at pages 63-66 for a discussion of procedures for screening for recombinants).

DEPR:
The present invention allows the manipulation of endothelial cell physiology by targeting expression of a substance in cells of the endothelial lineage in a mammal. The above described methods, transgenic animals and cell cultures derived therefrom, can therefore be used to assess the role of a substance in the determination, migration, or proliferation of cells of the endothelial lineage. In particular, the invention provides a mechanism for investigating vascularization of tumors and the control of angiogenesis. A transgenic mammal may be produced which expresses a substance exclusively in cells of

the endothelial lineage. A comparison of endothelial phenotype, morphology, and function using for example immunohistochemical techniques and assays for LDL receptors, and of the pattern and extent of expression of the substance in the animal with a control transgenic animal will provide an indication of the affect of the substance on cells of the endothelial lineage.

DEPR:
Comparison with other tyrosine kinases (FIG. 14) reveals that the deduced tek amino acid sequence shows 42% sequence identity to the mouse fibroblast growth factor receptor Flg (Reid et al., 1990; Safran, A., Avivi, A., Orr-Urtereger, A., Neufeld, G., Lonai, P., Givol, D. & Yarden, Y. (1990). Oncogene5, 635-643, Sambrook, J., Fritsch, E. F. & Maniatis, T. (1989). Molecular Cloning. Cold Spring Harbor Laboratory Press) and 45% to the transmembrane RTK encoded by the human c-ret protooncogene (Takahashi & Cooper, 1987). In addition, striking sequence identity is observed to a 65 amino acid residue sequence encoded by Jtk14, a putative tyrosine kinase cDNA isolated from differentiating human K562 cells by RT-PCR (Partanen et al., 1990). Taken together, the results suggest that tek encodes a novel RTK.

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Search Results - Record(s) 1 through 8 of 8 returned.

☐ 1. Document ID: US 6147106 A

L5: Entry 1 of 8 File: USPT Nov 14, 2000

US-PAT-NO: 6147106
DOCUMENT-IDENTIFIER: US 6147106 A
TITLE: Indolinone combinatorial libraries and related products and methods for the treatment of disease

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6025157 A

L5: Entry 2 of 8 File: USPT Feb 15, 2000

US-PAT-NO: 6025157
DOCUMENT-IDENTIFIER: US 6025157 A
TITLE: Neurturin receptor

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 6025192 A

L5: Entry 3 of 8 File: USPT Feb 15, 2000

US-PAT-NO: 6025192
DOCUMENT-IDENTIFIER: US 6025192 A
TITLE: Modified retroviral vectors

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 4. Document ID: US 5998187 A

L5: Entry 4 of 8 File: USPT Dec 7, 1999

US-PAT-NO: 5998187
DOCUMENT-IDENTIFIER: US 5998187 A
TITLE: Receptor tyrosine kinase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 5. Document ID: US 5882923 A

L5: Entry 5 of 8 File: USPT Mar 16, 1999

US-PAT-NO: 5882923
DOCUMENT-IDENTIFIER: US 5882923 A
TITLE: Glial cell line-derived neurotrophic factor regulation of ureteric budding and growth

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 6. Document ID: US 5808036 A

L5: Entry 6 of 8 File: USPT Sep 15, 1998

US-PAT-NO: 5808036
DOCUMENT-IDENTIFIER: US 5808036 A
TITLE: Stem-loop oligonucleotides containing parallel and antiparallel binding domains

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 7. Document ID: US 5681714 A

L5: Entry 7 of 8 File: USPT Oct 28, 1997

US-PAT-NO: 5681714
DOCUMENT-IDENTIFIER: US 5681714 A
TITLE: Nucleic acid encoding tek receptor tyrosine kinase

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 8. Document ID: US 5514546 A

L5: Entry 8 of 8 File: USPT May 7, 1996

US-PAT-NO: 5514546
DOCUMENT-IDENTIFIER: US 5514546 A
TITLE: Stem-loop oligonucleotides containing parallel and antiparallel binding domains

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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USPT	l1 and (antibody or antibodies)	14	L2
USPT	c-ret or c ret or cret	93	L1